Amendments to the Claims

Claim 1 (currently amended): A cytochrome C-reporter fusion protein construct comprising:

(a) a modified cytochrome C protein or any functional analogue thereof derived from wild type cytochrome C[[,]]; and

(b) a reporter, wherein said modified cytochrome C targets the mitochondria and has a reduced ability to induce apoptosis in a living cell.

Claim 2 (currently amended): The fusion construct of claim 1, wherein ~~the~~ said modified cytochrome C binds apoptosis protease activation factor-1 (Apaf-1) at least ten times less than wild type cytochrome C.

Claim 3 (currently amended): The fusion construct of claim 1 ~~or 2~~, wherein ~~the~~ said modified cytochrome C binds apoptosis protease activation factor-1 (Apaf-1) at least 100 times less than wild type cytochrome C.

Claim 4 (currently amended): The fusion construct of ~~any preceding~~ claim 1, wherein ~~the~~ said modified cytochrome C binds apoptosis protease activation factor-1 (Apaf-1) at least 1000 times less than wild type cytochrome C.

Claim 5 (currently amended): The fusion construct of ~~any preceding~~ claim 1, wherein at least one of the amino acids of ~~the~~ said modified cytochrome C at positions 4, 7, 8, 25, 39, 62, 63, 64, 65 and 72 has been mutated relative to the wild type cytochrome C.

Claim 6 (currently amended): The fusion construct of claim 5, wherein ~~the~~ said modified cytochrome C has an amino acid substitution or substitutions selected from the group consisting of K4E, K72A, K72L, K72R, K72G, K72X, E62N, K7E-K8E, K25P-K39H, K7A-E62N-K25P, K7A-E62N-K39H, K7E-K8E-E62N, K7A-K25P-E62N, K7A-E62N-K25P-K39H, E62N-T63N-L64M-M65S, K7E-K8E-E62N-K25P-K39H, K7E-K8E-K25P-E62N-T63N-L64M-M65S, K7E-K8E-K39H-E62N-T63N-L64M-M65S and K7E-K8E-K25P-K39H-E62N-T63N-L64M-M65S.

Claim 7 (currently amended): The fusion construct of claim 6, wherein ~~the~~ said modified cytochrome C comprises the amino acid ~~substitution~~ substitutions selected from the group consisting of K7E-K8E-E62N-K25P-K39H, K7E-K8E-K25P-E62N-T63N-L64M-M65S, K7E-K8E-K39H-E62N-T63N-L64M-M65S and K7E-K8E-K25P-K39H-E62N-T63N-L64M-M65S.

Claim 8 (currently amended): The fusion construct of claim 6, wherein ~~the~~ said modified cytochrome C comprises the amino acid substitution selected from the group consisting of K72A, K72L, K72R, K72G and K72X, wherein X represents trimethylation.

Claim 9 (currently amended): The fusion construct of ~~either of claims 6 or 8~~ claim 6, wherein ~~the~~ said modified cytochrome C comprises the amino acid substitution K72A or K72L.

Claim 10 (currently amended): The fusion construct of claim 6, wherein ~~the~~ said modified cytochrome C comprises the amino acid substitution K4E.

Claim 11 (currently amended): The fusion construct of ~~any preceding~~ claim 1, wherein ~~the~~ said reporter is a fluorescent protein or a functional analogue thereof.

Claim 12 (original): The fusion construct of claim 11, wherein said fluorescent protein is selected from the group consisting of Green Fluorescent Protein (GFP), Yellow Fluorescent Protein (YFP), Blue Fluorescent Protein (BFP), Cyan Fluorescent Protein (CFP), Red Fluorescent Protein (RFP), Enhanced Green Fluorescent Protein (EGFP) and Emerald.

Claim 13 (currently amended): The fusion construct of ~~either of claims 11 or 12~~ claim 11, wherein ~~the~~ said fluorescent protein is Enhanced Green Fluorescent Protein or Emerald.

Claim 14 (currently amended): The fusion construct of claim 11, wherein ~~the~~ said GFP comprises:

i) an amino acid substitution at position F64L;

ii) an amino acid substitution at position S175G; and

iii) an amino acid substitution at position E222G.

Claim 15 (currently amended): The fusion construct of ~~any preceding~~ claim 1 selected from the group consisting of SEQ ID NO: 4 and SEQ ID NO: 6.

Claim 16 (currently amended): The fusion construct ~~according to any of claims 1 to 10~~ of claim 1, wherein the reporter is localisable by a detectable luminescent, fluorescent or radio-active moiety.

Claim 17 (currently amended): The fusion construct ~~according to~~ of claim 16, wherein the reporter comprises an immunogenic motif.

Claim 18 (currently amended): The fusion construct ~~according to claim 15 or 16~~ of claim 16, wherein the reporter comprises a cysteine-rich motif.

Claim 19 (currently amended): The fusion construct ~~according to~~ of claim 16, wherein said detectable moiety comprises a bi- arsenical compound.

Claim 20 (currently amended): The fusion construct ~~according to~~ of claim 16, wherein said moiety comprises an antibody.

Claim 21 (currently amended): A nucleotide sequence encoding ~~a~~ the fusion construct of claim 1 ~~any of the preceding claims~~.

Claim 22 (currently amended): A nucleotide sequence ~~encoding a fusion construct according to claim 15~~ selected from the group consisting of SEQ ID NO: 3 and SEQ ID NO 5.

Claim 23 (currently amended): A nucleic acid construct comprising a suitable control region and ~~a~~ the nucleotide sequence ~~according to~~ of claim 21 ~~or 22~~, said sequence being under the control of said control region.

Claim 24 (currently amended): ~~A~~ The nucleic acid construct ~~according to~~ of claim 23 being under the control of a promoter selected from the group consisting of native cytochrome C promoter, mammalian constitutive promoter, mammalian regulatory promoter, human ubiquitin C promoter, viral promoter, SV40 promoter, CMV promoter, yeast promoter, filamentous fungal promoter and bacterial promoter.

Claim 25 (currently amended): ~~A~~ The nucleic acid construct ~~according to~~ of claim 24, wherein said viral promoter is the CMV or the SV40 promoter.

Claim 26 (currently amended): ~~A~~ The nucleic acid construct ~~according to~~ of claim 24, wherein the promoter is the human ubiquitin C promoter.

Claim 27 (currently amended): A replicable vector comprising ~~a~~ the nucleic acid construct of claim 23 ~~according to any of claims 23 to 26~~.

Claim 28 (original): The replicable vector of claim 27, wherein said vector is a plasmid vector.

Claim 29 (original): The replicable vector of claim 27, wherein the vector is a viral vector.

Claim 30 (original): The replicable vector of claim 29, wherein said viral vector is selected from the group consisting of cytomegalovirus, Herpes simplex virus, Epstein-Barr virus, Simian virus 40, Bovine papillomavirus, Adeno-associated virus, Adenovirus, Vaccina virus and Baculovirus vector.

Claim 31 (currently amended): A host cell stably transformed with ~~a~~ the nucleic acid construct of claim 23 ~~according to any of claims 23 to 26~~.

Claim 32 (currently amended): A host cell transiently transformed with ~~a~~ the nucleic acid construct of claim 23 ~~according to any of claims 23 to 26~~.

Claim 33 (currently amended): The host cell of ~~claims 31 or 32~~ claim 31 selected from the group consisting of plant, insect, nematode, bird, fish and mammalian cell.

Claim 34 (original): The host cell of claim 33, wherein said mammalian cell is a human cell.

Claim 35 (original): The host cell of claim 34, wherein said human cell is selected from the group consisting of Hek, HeLa, U2OS and MCF-7.

Claim 36 (original): The host cell of claim 35, wherein said Hek cell is Hek293.

Claim 37 (currently amended): The host cell ~~according to any of claims 31 to 36~~ of claim 31 capable of expressing the fusion protein of claim 1 ~~any of claims 1 to 20~~.

Claim 38 (currently amended): A method for detecting apoptosis in a living cell comprising the steps of:

i) culturing a cell transformed to over-express ~~a~~ the fusion construct of claim 1 ~~according to any of claims 1 to 20~~; and

ii) determining the localisation of the fusion construct within the cell with time;

wherein a change in localisation of the fusion construct within the cell is indicative of apoptosis.

Claim 39 (currently amended): A method for measuring the effect that an agent has upon modulating apoptosis in a living cell comprising the steps of:

i) culturing a cell transformed to over-express ~~a~~ the fusion construct of claim 1 ~~according to any of claims 1 to 20~~;

ii) determining the localisation of said construct within the cell;

iii) treating the cell with said agent and determining the localisation of the construct within the cell;

wherein any difference in the localisation of the construct within the cell relative to control cells untreated with the agent is indicative of the effect that the agent has upon modulating apoptosis.

Claim 40 (currently amended): A method for measuring the effect an agent has upon modulating apoptosis in a living cell comprising the steps of:

i) culturing a first cell and a second cell which both over-express ~~a~~ the fusion construct of claim 1 ~~according to any of claims 1 to 20~~;

ii) treating said first cell with said agent and determining the localisation of said construct within the first cell;

iii) determining the localisation of the construct within said second cell which has not been treated with the agent;

wherein any difference in the localisation of the construct within the first cell and second cell is indicative of the effect that the agent has upon modulating apoptosis.

Claim 41 (currently amended): A method for measuring the effect an agent has upon modulating apoptosis in a living cell comprising the steps of:

i) culturing a cell transformed to over-express ~~a~~ the fusion construct of claim 1 ~~according to any of claims 1 to 20~~;

ii) treating said cell with said agent and determining the localisation of the construct within the cell;

iii) comparing the localisation of the construct in the presence of the agent with a known value for the localisation of the construct in the absence of the agent;

wherein any difference in the localisation of the construct within the cell in the presence of the agent and said known value in the absence of the agent is indicative of the effect that the agent has upon modulating apoptosis.

Claim 42 (currently amended): The method ~~according to~~ of claim 41, wherein the known value is stored on a database.

Claim 43 (currently amended): The method of claim 38-41 ~~according to any of claims 38 to 42~~, wherein the localisation of said fusion construct is measured by its luminescence, fluorescence or radioactive properties.

Claim 44 (currently amended): The method of claim 39-41 ~~according to any of claims 39 to 43~~, wherein said agent induces apoptosis.

Claim 45 (currently amended): The method of claim 39-41 ~~according to any of claims 39 to 43~~, wherein the agent inhibits apoptosis.

Claim 46 (currently amended): The method of claim 38-41 ~~according to any of claims 38 to 45~~, wherein the localisation of the protein fusion is determined following fixation of the cells.

Claim 47 (currently amended): The method of claim 38-41 ~~according to any of claims 38 to 46~~, where the agent is a chemical, physical or biological agent.